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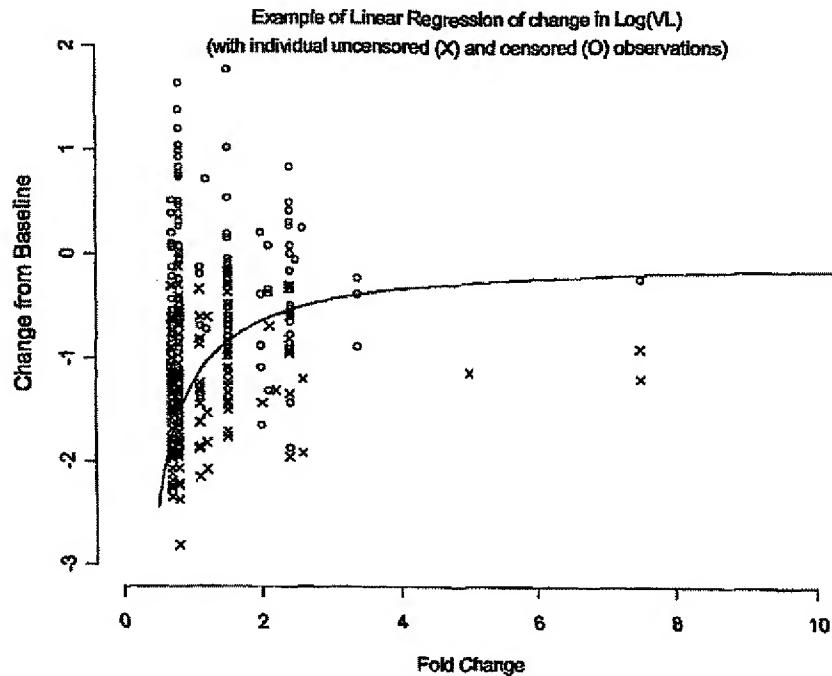
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[Continued on next page]

(54) Title: ESTIMATION OF CLINICAL CUT-OFFS



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(57) Abstract: Methods and systems for improving the accuracy of predicting resistance of a disease to a drug are described. More specifically, methods for assessing the impact of pre-existing variations in drug susceptibility, whether naturally occurring or selected by previous drug exposure, on treatment response in order to establish clinically relevant cut-off values for phenotypic or genotypic resistance tests are described.



European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,*

HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations of inventorship (Rule 4.17(iv)) for US only*

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/050888

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G06F19/00 C12Q1/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G06F C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, IBM-TDB, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HARRIGAN P R ET AL: "World-wide variation in HIV-1 phenotypic susceptibility in untreated individuals: biologically relevant values for resistance testing." AIDS (LONDON, ENGLAND) 7 SEP 2001, vol. 15, no. 13, 7 September 2001 (2001-09-07), pages 1671-1677, XP008053108 ISSN: 0269-9370 cited in the application abstract; figures 1,2,4; table 1 page 1672, left-hand column, paragraph 3 – page 1674, left-hand column, paragraph 1</p> <p>-----</p> <p style="text-align: center;">-/-</p>	22-25

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/79540 A (VIRCO N.V; LARDER, BRENDAN; BLOOR, STUART; HERTOGS, KURT; DEHERTOGH, P) 25 October 2001 (2001-10-25) cited in the application the whole document -----	22-25
X	TURAL CRISTINA ET AL: "Clinical utility of HIV-1 genotyping and expert advice: the Havana trial." AIDS (LONDON, ENGLAND) 25 JAN 2002, vol. 16, no. 2, 25 January 2002 (2002-01-25), pages 209-218, XP008053107 ISSN: 0269-9370 abstract page 210, left-hand column, paragraph 1 - page 212, right-hand column, last paragraph page 217, left-hand column, paragraph 2 -----	22-25
P,X	WO 2004/111907 A (VIRCO BVBA; VAN MARCK, HERWIG, GASTON, EMIEL; VAN DEN BULCKE, TIM, GER) 23 December 2004 (2004-12-23) abstract; claims 1,8,11,13-16; figure 1 page 3, line 23 - page 5, line 28 page 1, lines 2-9 page 7, line 5 - page 9, line 5 page 16, line 17 - page 21, line 28 -----	22-25

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 1-21
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/050888

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 0179540	A 25-10-2001	AU 6022401	A 30-10-2001	
		CA 2406140	A1 25-10-2001	
		EP 1332231	A2 06-08-2003	
		JP 2004500836	T 15-01-2004	
WO 2004111907	A 23-12-2004	NONE		